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Central Neurogenic Hyperventilation with Pontine Tumor. Case Report and a Review of the Literature

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Summary

Nine cases of brain tumor presenting central neurogenic hyperventilation have been reported previously. We report the tenth such case. The patient is a 7-year-old girl harboring a brainstem glioma. She presented with severe hyperventilation, but later regained the near-normal respiratory pattern. The extent of the tumor was depicted for the first time by magnetic resonance imaging. Mechanism of central neurogenic hyperventilation with brainstem lesions is briefly discussed.

Central neurogenic hyperventilation is a rare condition. It is defined as a clinical entity showing decreased arterial carbon dioxide tension ($PaCO_2$), normal or increased arterial oxygen tension (PaO_2), and alkalosis in the absence of pulmonary or peripheral chemoreceptor reflex acceleration (6). Only nine confirmative cases of brain tumor presenting central neurogenic hyperventilation have been reported previously (1,2,4,6–10), and this condition has been believed to indicate an invariably poor prognosis.

Recently we have seen a girl with brainstem glioma, in whom central neurogenic hyperventilation was seen but was reversible. In this paper, we report this case briefly and summarize the clinical and anatomical features of ten reported cases including ours.

Case Report

A 7-year-old girl was first seen on July 29, 1986, with a one-month history of gait disturbance, dysphagia, and dysarthria. On admission, neurological examination found weakness of the bilateral abducens and left hypoglossal nerves, left supranuclear facial paresis, dysphagia and

Key words: Astrocytoma, Brainstem, Hyperventilation, Hypocapnea, Magnetic resonance imaging, Respiratory center.
索引用語：星細胞腫，脳幹腫瘍，過換気，血中炭酸ガス分圧低下，磁気共鳴画像，呼吸中枢.
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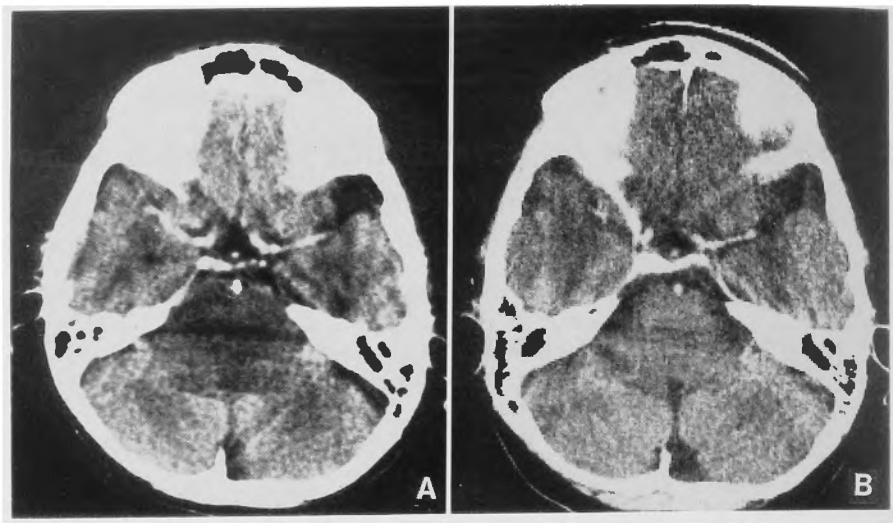

Fig. 1. (A) Enhanced axial CT scan on initial admissison, showing lucent, non-enhancing enlargement of the pons. (B) Enhanced axial CT scan after irradiation, showing restoration of normal size and attenuation of the pons.

ataxia of gait. Deep tendon reflexes were exaggerated in the lower extremities and Babinski sign was positive bilaterally.

Results of the routine laboratory tests were entirely within the normal limits. Computed tomography (CT) scan demonstrated diffuse enlargement of the pons, which was hypodense and did not enhance (Figure 1 A). The extent of the lesion involving the pons and the medulla oblongata was better shown by magnetic resonance (MR) imaging (Figure 2A).

The patient received a radiation therapy (50 Gy) and her condition improved rapidly. On discharge seven weeks after admission, she was neurologically normal except for a diplopia on

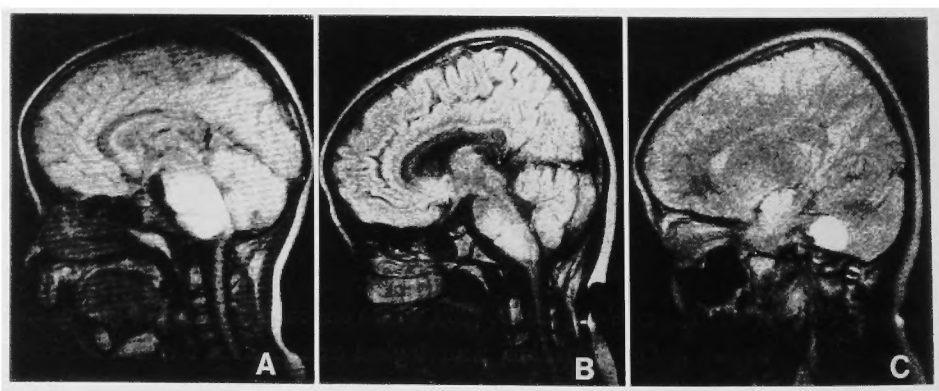

Fig. 2. (A) Midsatital MR image (0.5 Tesla, TR 1500/TE40) showing high intensity signal lesion in the pons and the medulla oblongata. (B & C) Follow-up MR images after irradiation, showing marked reduction in the size and the intensity signal of the lesion in B (0.5 Tesla, TR 2000/TE43), and an exophytic mass of high intensity signal in the cerebellopontine angle region in C (0.5 Tesla, TR1500/TE80).

the extreme right lateral gaze. Repeated CT scan showed restoration of the size and density of the pons toward the near-normal (Figure 1B). MR imaging also showed marked reduction in the size of the lesion (Figure 2B). On the T2-weighted image, however, a round exophytic mass with high intensity signal was found in the right cerebellopontine angle (Figure 2C).

On October 2, the patient returned with quadriparesis and uncontrollable hyperpnea, which appeared and rapidly progressed since the day before this admission. She had been receiving no stimulating drugs. She was lethargic but easily arousable and she often became agitated and restless. Her hands and feet were cold and cyanotic. Neurological examination found flaccid tetraparesis which was more marked on the right side and a right central facial paresis. Her pupils were round, isocoric, and reacted normally to light. Her respiration was regular but the respiratory rate reached 42 to 52 breaths per minute. Her heart and lungs were clear on auscultation, and chest roentgenograms and electrocardiograms were normal. The arterial blood gases taken while breathing room air were highly abnormal; PaO_2=124.6 torr, $PaCO_2$=7.7 torr, pH=7.58, and the base deficit=8.4 mEq/liter. Methylprednisolone (125 mg) and diazepam (5 mg) were intravenously given. On forced rebreathing from a bag for one hour, the repeated arterial blood gas analysis showed some improvements; PaO_2=114.7 torr, and $PaCO_2$=14.5 torr.

Methylprednisolone was given for four days in a dose of 125 to 250 mg per day. Her tetraparesis gradually subsided in two days, but her hyperventilation (32 to 40 breaths per minute) persisted during both wakefulness and sleep for four days. On October 5, 3 days after the readmission, the arterial blood gases on room air were much improved; PaO_2=97 torr, $PaCO_2$=29 torr, pH=7.50, and the base excess=1.4 mEq/liter. MR imaging repeated on the second admission (Figure 3A, B, C) demonstrated two exophytic extensions of the tumor, one in the right cerebellopontine angle region and the other in the left premedullary area.

Right suboccipital craniectomy was performed in the lateral position. A needle puncture of the right cerebellopontine angle mass yielded the yellowish clear fluid which did not clot on standing at a room temperature. The partially cystic exophytic tumor was removed subtotally.

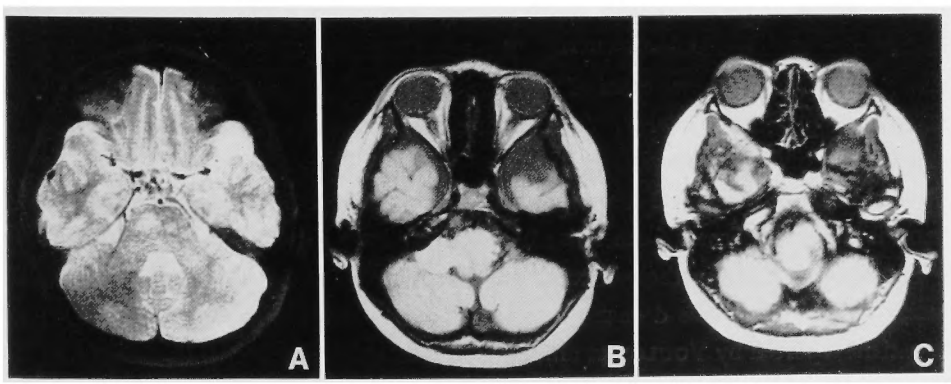

Fig. 3. MR images on second admission, showing two exophytic extensions of the lesion (B & C, 1.5 Tesla, TR2000/TE20). Upper part of the intraaxial tumor is seen in A (TR2000/TE80).

Histological diagnosis was a pilocytic astrocytoma with scanty foci of mild endothelial proliferation. Her condition improved, and she was discharged on November 12, with a residual mild right facial paresis. Three months later, her neurological condition was stable on 0.5 mg/day dose of betamethasone, and she was doing well at school and home. Her respiration was still slightly shallow, with the rate of 24 breaths per minute.

Discussion

In 1959 PLUM and SWANSON proposed the existence of "central neurogenic hyperventilation" based on the observation of 9 patients with brainstem infarct. All these patients showed a type of hyperventilation accompanying profound hypocapnia and arterial alkalosis in the absence of anoxemia. The lesions common to the autopsied cases involved the medial pons, sparing the lateral pontine region and the medulla oblongata. Initially Plum and Swanson thought that the disconnection of the otherwise normal medullary respiratory centers from regulatory control originating in the cortex, the thalamus, or the pons was responsible for this peculiar type of hyperventilation[6].

However, PLUM later developed another thoughts about the validity of their previous conclusions[7]. As all of the autopsied cases in their previous series[6] had congestion of the lungs and the arterial blood oxygen concentrations measured during life were subnormal when the patients were removed from an increased oxygen concentration in the inspired air, he thought that the hyperpnea could have reflected the presence of increased afferent drives to breathing arising from the lungs and from the arterial chemoreceptors, a process very much different from a true central (nonreflex) hyperpnea. PLUM further stated, "to qualify for the diagnosis of central neurogenic hyperventilation, patients should not be receiving stimulating drugs; their blood gases taken while breathing room air should show low $PaCO_2$, high PaO_2, and elevated arterial pH, and the abnormality should persist during sleep"[7]. Our present case evidently fulfil all these requisites for the clinical diagnosis of central neurogenic hyperventilation.

As far as we adhere rigidly to PLUM's criteria cited above, reports of the definitive cases of central neurogenic hyperventilation are extremely rare. Reviewing the literature, we could collect only nine such cases[1,3,5,7,8,9,10,11]. Ten cases including the present one are summarized in Table 1. If one accepts two cases of PLUM without histological verification, six out of a total of ten cases had pontine glioma. Three other cases had primary lymphoma and one had lymphomatoid granulomatosis.

The mechanism of central neurogenic hyperventilation initially proposed by PLUM and SWANSON is a disconnection of otherwise normal medullary respiratory centers from the regulatory control originating in the cortex, the thalamus, or the pons[6]. It has been pointed out, however, that this hypothesis does not necessarily fit to the lesion found in the reported cases. In the patient reported by VOULON et al., the astrocytoma had infiltrated the medullary and the pontine tegmentum but the nuclear structures were well preserved[3]. RODRIGUEZ et al. reported a 53-year-old man who showed central neurogenic hyperventilation ($PaCO_2$ of 9 torr) with a normal level of consciousness that lasted for 8 days. In this patient, the entire extent of the

Table 1. Summary of 10 reported cases of central neurogenic hyperventilation with brainstem tumor.

No	Author	Year	Age*/ Sex	Consciousness during attack	Blood gas			Histology	Extent of tumor	Outcome
					$PaCO_2$#	PaO_2#	pH			
1	Suzuki	1964	5/M	coma	—	—	7.47	astrocytoma	pontine to medullary tegmentum	death
2	Lange	1965	51/M	alert	12	—	7.58	primary lymphoma	midbrain, pons, meninges	death
3	Goulon	1969	22/F	alert	7	—	7.71	astrocytoma	pontine to medullary tegmentum	death
4	Tinaztepe	1981	7/M	alert	—	—	7.52	primary lymphoma	cortex, peduncles, pons, medulla, meninges	death
5	Rodriguez	1982	53/F	alert	9	121	7.74	astrocytoma	medudlla, pontine tegmentum, midbrain, cerebellum, trigeminal nerve	death
6	Plum	1982	8/M	alert	9	105	7.47	—	pons (by PEG)	death
7	Plum	1982	39/M	alert	27	94	7.51	—	pons (by CT)	death
8	Sunderrajan	1984	41/M	alert	7	120	7.62	lymphomatoid granulomatosis	cerebral hemisphere (by CT)	alive
9	Bateman	1985	62/F	drowsy	12	116	7.61	primary lymphoma	cortex, hypothalamus, midbrain, meninges	death
10	Nakasu	1988	7/F	drowsy	7.7	125	7.58	astrocytoma	pons, medulla	alive

* Age in years, # mmHg

medulla oblongata was involved with the astrocytoma as were the tegmentum of the pons, the brachia conjunctiva, and the white matter of the cerebellar hemisphere, but there were no structural derrangements in the nuclei of the brainstem[8]. BATEMAN further stated that the direct destruction of the brainstem respiratory centers was unnecessary for the development of central neurogenic hyperventilation[1]. Experimental evidence also indicates that the destruction of the lower brainstem has never caused typical neurogenic hyperventilation in animals[1].

PLUM has suggested an alternate mechanism that ascribes central neurogenic hyperventilation to the local stimulation of chemosensitive areas by hydrogen ions produced by neoplastic cells[7]. Local acidification of the cerebrospinal fluid in the region of the brainstem caused by the metabolizing tumor cells is a possibility, because meningeal infiltration by tumor cells were found in several cases of central neurogenic hyperventilation reported previously[1,5]. BATEMAN, however, has pointed out that central neurogenic hyperventilation is extremely rare, although the meningeal infiltration of cancer cells that may cause local submeningeal acidification is a popular pathological finding[1].

It is believed that the destruction of the brainstem nuclei or tracts regulating ventilation does not cause a reversible and transient hyperventilation as seen in three patients including our case[9,10]. In the present patient, the main locus of the tumor is the ventral portion of the lower pons and the medulla oblongata, but the extent of the peritumoral edema and possibly the

tumor infiltration are apparently more diffuse, and they might have damaged the respiratory center in the pontine tegmentum. On one hand, the exophytic growth of the tumor might have been a source of hydrogen ion accumulation in the local cerebrospinal fluid space. However, this hypothesis also hardly explains the reversibility of hyperventilation in this child.

Local mild changes in metabolism or circulation in the upper suppressive respiratory center anywhere from the cerebrum to the pons are the alternate mechanism that could change the rhythm of ventilation. Such changes may be reversible or irreversible according to the severity of the damage. Central neurogenic hyperventilation in the present patient subsided in five days. Such an improvement in respiratory rhythm may suggest that the metabolic or microcirculatory changes in the brainstem could be improved, possibly by steroid therapy.

It seems interesting to note here that seven of the ten reported cases of central neurogenic hyperventilation were alert in the face of extremely low $PaCO_2$ (Table 1). Two other patients were lethargic, and the remaining patient reported by SUZUKI et al.[10] showed repeated episodes of hyperventilation associated with disturbance of consciousness. There is the evidence that at the $PaCO_2$ level of 20 torr, the cerebral blood flow is so low that the threshold for sustaining normal neuronal function is practically reached[3]. Although the cerebral blood flow has not been measured in any of these 10 patients with central neurogenic hyperventilation, the brainstem must have suffered from very low blood flow, and the maintenance of consciousness is difficult to explain.

References

1) Bateman DE, Gibson GJ, Hudgson P, et al: Central neurogenic hyperventilation in a conscious patient with a primary cerebral lymphoma. *Ann Neurol* **17**: 402–405, 1985.
2) Casanova MF: Vasogenic edema with intraparencymatous expanding mass lesions: a theory on its pathophysiology and mode of action of hyperventilation and corticosteroids. *Med Hypothesis* **13**: 439–450, 1984.
3) Goulon M, Escourolle R, Augustin P, et al: Hyperventilation primitive par gliome bulbo-protuberantiel. *Rev Neurol (Paris)* **121**: 636–639, 1969.
4) Harp JR, Wollman H: Cerebral metabolic effects of hyperventilation and deliberate hypotension. *Br J Anesth* **45**: 256–258, 1973.
5) Lange LS, Laszlo G: Cerebral tumour presenting with hyperventilation. *J Neurol Neurosurg Psychiatry* **28**: 317–319, 1965.
6) Plum F, Swanson AG: Central neurogenic hyperventilation in man. *AMA Arch Neurol Psychiatry* **81**: 535–549, 1959.
7) Plum F: Mechanisms of "central hyperventilation". *Ann Neurol* **11**: 636–637, 1982
8) Rodriguez M, Baele PL, Marsh HM, et al: Central neurogenic hyperventilation in an awake patient with brainstem astrocytoma. *Ann Neurol* **11**: 625–628, 1982.
9) Sunderrajan EV, Passamonte PM: Lymphomatoid granulomatosis presenting as central neurogenic hyperventilation. *Chest* **86**: 634–636, 1984.
10) Suzuki M, Kawakatsu T, Kamoshita S, et al: A case of pontine tumor associated with repeated episodes of hyperventilation and ketosis. *Clin Neurol (Tokyo)* **4**: 54–59, 1964.
11) Tinaztepe B, Tinaztepe K, Yalaz K, et al: Microgliomatosis presenting as sustained hyperventilation. *Turkish J Pediat* **23**: 269–275, 1981.

和文抄録

橋腫瘍でみられた中枢性過換気：症例報告と文献考察

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厳密な定義による中枢性過換気は稀な病態で，現在まで，脳腫瘍で中枢性過換気を示したものの報告は9例にすぎない．我々は，橋腫瘍で強度の中枢性過換気を示し，正常呼吸に復し得た症例を経験した．症例は7歳女性で，歩行障害を主訴に来院し，CT スキャン，MRI にて橋腫瘍と診断された．放射線治療後，軽快退院したが，約2週間後に過呼吸をきたすようになり再入院．入院時，$PaCO_2$ 7.7 mmHg と強度の過呼吸を示し，睡眠中も持続した．この症状は，ステロイド剤等の投与で4日程で軽快した．再入院時 MRI で認められた小脳橋角部に突出した部を手術的に摘出し，組織診断は星細胞腫であった．中枢性過換気の病因について文献的考察を加えた．